Inductive Electric Fields Applied to ESI & MALDI, Supporting Protein Therapeutic Characterizations & QC.

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Be it for the characterization of a therapeutic, process characterization and QC, glycan profiling, peptide mapping, characterization of isoforms or other analytes (amino acid analysis), the production and QC of new therapeutics offers ma**n**y challenges across the field of mass spectroscopy and analytical chemistry in general. Here we address how inductive electric (IEF) have been and can be used to aid qualitative and quantitative MS analysis, http://nanoliter.com/references2015.pdf.

For MALDI, IEF have been used by Gross, Harmon, Yergey, Gillen, Stretton, Cody, and others, to increase the sensitivity of MALDI, SIMS and DART by greater than one order of magnitude when nLs are generated via IEF and compared to analysis of uL volumes of samples of proteins, peptides, industrial polymers, explosives , drugs, and Lanthanide metals chelates, acquired identically, a very counter-intuitive observation. T. Tu, M. L. Gross, et al, showed that using IEF for MALDI TOF, Bradykinin was 20x more sensitive using 20 nL depositions as compared 0.5 uL sample size, acquired identically. Harmon had similar increased sensitivity observations for MALDI of polymers, and Yergey observed in it's first application at NIH, a never before PTM of a tublin (glycosylation) in actual NIH brain cancer samples using IEF to dispense nanoliter quantities of sample, as compared to uL quantities. It was estimated that the IEF MALDI data was 10-100x more sensitive when nL samples volumes were employed in this application. Similarly at Wisconsin, Stretton et al, employed IEF to perform single cell MALDI identifying six never before known ocular proteins, due in part to the increase in sensitivity, and also due to the ability to use IEF to direct a droplet of matrix to the target, as compared to using a dispersive spray.

IEF can also be used to place 100% of liquid samples in millisecond, timeframes into ESI mass spectrometers shooting droplets like this…… in a straight line, producing ion current from droplets out of a "zero" background. This differs from spraying the sample all over creation with ca. <1% introduction efficiency, from a high background. Recently, Ross and Limbach published that IEF droplets can be used to improve the MS analysis of oligonucleotides. Spectra acquired from droplets, as opposed to a spray, yielded ion current ratios that agreed with known molar quantities (1:1) where the spray mode did not (1:3). This and other data points to the hypothesis that droplet streams desolvate better than sprays, as more work ensues. Using IEF, Groenewold also analyzed 30 chelates of the entire Lanthanide series in +eV and –eV in milliseconds with 100% sample introduction efficiency at ca. 10 nLs/sec and faster, yielding Lanthanide isotope ration in excellent agreement with known values. Data was acquired at sample analysis rates of 2 Hz via an old XP ion trap **WITHOUT** an ICP, funnels or ion optic optimization realizing low fg levels. Also, IEF were used to shoot electrolytes into a MS from an OPERATING battery!

IEF were used by Scheeline at Illinois for a pure science application, where droplets fired and directed by induction were shot into levitated droplets, in millisecond timeframes to study wall-less reaction kinetics. Such common and uncommon applications of IEF affords new MS configurations and approaches to address the analytical challenges in the area of protein therapeutics and analytical chemistry, be it for the speed of analysis, sensitivity or unique analytical analysis IEF configurations.

Because fast droplet generation and dynamics are not widely understood, we summarize the physics of IEF for MS sample introduction and placement from different Gaussian surfaces (i.e., LC columns to syringes, pipettes, chips). We discuss how the effective "printing" of samples into and onto targets can aid complex mixture analysis and problems implicit in Protein Therapeutics discovery and production.